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## Public Health Surveillance of Prenatal Opioid Exposure in Mothers and Infants

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### Abstract

The US opioid crisis is the public health emergency of our time and requires urgent public health action to monitor and protect the most vulnerable Americans. We have witnessed a startling death toll in 2017 with 70 237 drug overdose deaths in the United States, of which two-thirds involved opioids.<sup>1</sup> The devastating consequences of this epidemic for mothers and infants have received less attention. Increases in opioid use and misuse in pregnancy have paralleled the increases in the general population; at delivery hospitalization, there were 4 times as many women with an opioid use disorder in 2014 compared with 1999.<sup>2</sup> One of the most immediate and visible impacts of the opioid crisis on infants is the drug withdrawal in the newborn period, termed neonatal abstinence syndrome (NAS). On the basis of 2014 data, 1 newborn was diagnosed with NAS every 15 minutes in the United States, totaling about 32 000 infants annually with associated hospital costs estimated at \$563 million.<sup>3</sup>

### INFORMING CLINICAL CARE AND LINKAGE TO SERVICES FOR PREGNANT WOMEN AND INFANTS

Because prevention and treatment of opioid use disorder in pregnancy is important to both maternal and infant health, there is an urgent need to expand prevention efforts and reduce barriers for medication-assisted treatment before, during, and after pregnancy. The stigma of substance exposure during pregnancy and fears of punitive consequences can be obstacles to women receiving the treatment and care they need, and studies with inadequate control of cofactors can exaggerate the specific effects of an individual substance as occurred with prenatal cocaine exposure.<sup>4</sup> Opioid use disorder during pregnancy is a medical condition that requires care and treatment and can have adverse consequences for the infant, much like pregestational diabetes, which increases the risk of birth defects and other adverse pregnancy outcomes.<sup>5</sup> Current recommendations for pregnant women with opioid use disorder are to

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avoid withdrawal during pregnancy and be provided appropriate opioid agonist treatment.<sup>6</sup> Increasing and targeting prevention efforts and providing appropriate treatment and adequate access to care could improve both maternal and infant health in the midst of this public health crisis.

Public health surveillance is needed to fill critical knowledge gaps and inform clinical guidance for the care of pregnant women with a treated or untreated opioid use disorder and their infants. Updated, evidencebased clinical guidance might help mitigate adverse infant and childhood outcomes by providing treatment that is tailored to the specific prenatal exposures, including both pharmacologic and nonpharmacologic treatments for infants who are exposed. Progress could be monitored by using a cascade of care model (Table 1) with metrics obtained from longitudinal linked public health surveillance.

## **UNDERSTANDING THE FULL IMPACT OF PRENATAL OPIOID EXPOSURE ON INFANTS AND CHILDREN**

Understanding the effects of prenatal opioid and polysubstance exposure requires assessing the multiple forms and combinations in which exposure can occur. Prenatal opioid exposure can include opioid medications for pain management or treatment of opioid use disorder, misuse of prescription or illicit opioid drugs, and polysubstance exposure to both opioids and other potentially harmful substances. Although NAS is a wellrecognized consequence of prenatal opioid exposure, the full impact of exposure to these psychoactive medications on the developing fetus and particularly the fetal brain is unknown; the effects might extend far beyond diagnoses that are apparent in the first days and weeks of life. Of significant concern is that polysubstance exposure during pregnancy can include alcohol, a known human teratogen. The lessons learned from prenatal alcohol exposure might be relevant for opioids. Although there is no known safe level of alcohol exposure in pregnancy, sustained and heavy use of alcohol in pregnancy can cause fetal alcohol spectrum disorders. Fetal alcohol spectrum disorders can include a range of physical problems (eg, facial features, central nervous system abnormalities) as well as neurologic (eg, executive functioning deficits), behavioral (eg, emotional lability), and learning disabilities, which are lifelong and influenced by timing and extent of exposure in pregnancy.<sup>7</sup> We are concerned that fetal opioid exposure (and fetal polysubstance exposure) might also result in a range of adverse outcomes and that not all will be readily apparent at birth. Prenatal alcohol exposure has been associated with onset of alcohol use disorders when the prenatally exposed children reach adolescence and young adulthood,<sup>8</sup> and it is suggested in animal studies that prenatal alcohol can also increase the risk of addiction to other drugs of abuse.<sup>9</sup> Public health surveillance could help inform whether a similar risk of future addiction affects children with prenatal exposure to opioids. As was true in evaluating prenatal cocaine exposure, full consideration must be given to the postnatal environment of children with prenatal opioid exposures, which might include social and economic complexities that adversely impact child development.

The full impact of opioid exposure during pregnancy on the health of our nation's children, including the impact on birth defects, is not yet known. The birth prevalence of

gastroschisis, a severe defect of the abdominal wall, has been increasing for more than a decade with no clear explanation. Young maternal age is the strongest and most consistent risk factor for gastroschisis. Prescription opioid exposure in early pregnancy has been associated with several structural birth defects, including gastroschisis, and authors of 1 recent study suggested a possible association between preconception opioid use and autism.<sup>10–12</sup> The Centers for Disease Control and Prevention released a report linking county-level opioid prescribing data with population-based birth defects surveillance data of gastroschisis from 20 states that include nearly 50% of US births.<sup>13</sup> Although the authors of the report use an ecological design with appropriate cautions for not overinterpreting this association, the prevalence of gastroschisis was 1.6 times higher in counties with high opioid prescribing rates (5.1 per 10 000 live births; 95% confidence interval: 4.9–5.3) compared with counties with low opioid prescribing rates (3.2 per 10 000 live births; 95% confidence interval: 3.1–3.4). The report sounds an early alarm for the need to increase our public health surveillance on the full range of fetal, infant, and childhood outcomes potentially related to these exposures. More research is needed to better understand the possible role of opioid exposure or related substance exposure on the occurrence of gastroschisis and other birth defects and the underlying mechanisms for these potential effects. Areas of the United States with high opioid use might need to plan for services for infants and children impacted with a broader range of adverse outcomes, far beyond the impact of NAS. Current surveillance efforts are limited to monitoring prenatal opioid use, opioid use disorder at delivery, and diagnosis of NAS; these efforts lack information on the full range of outcomes that could be obtained from longitudinal mother-infant linked surveillance approaches.

## A PUBLIC HEALTH CALL TO ACTION

There is an urgent need to build the evidence base and define the full spectrum of adverse infant and childhood outcomes associated with sustained prenatal opioid exposure and monitor the linkage to needed care and services. Longitudinal linked surveillance of mother-infant pairs with follow-up into childhood will help clarify the physical and developmental health outcomes linked to prenatal opioid exposure and help target effective programs and services to mitigate adverse effects of the substance exposure. Some preliminary data suggest that infants with a diagnosis of NAS are more likely to need special education services in preschool and early school age than infants without this diagnosis, but better data are needed to clarify the nature of the developmental problems and how they might relate to in utero exposures to opioids and other substances as well as the postnatal environment.<sup>14</sup> The Centers for Disease Control and Prevention collaborated with clinical and public health partners to launch mother-infant linked surveillance during the Zika virus emergency to rapidly understand the impact of infection during pregnancy and translate findings to action in the form of clinical guidance.<sup>15</sup> We are committed to building on this model to continue to address the health threats to and needs of mothers and infants through a network of public health surveillance.

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## ABBREVIATION

NAS neonatal abstinence syndrome

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**TABLE 1**

**Proposed Cascade of Care for Prenatal Opioid Exposure and the Impact on Mothers and Infants**

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**Cascade of Care**

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Reproductive-aged women with opioid use disorder at risk for pregnancy

Pregnant women with opioid use disorder

Pregnant women with opioid use disorder linked to treatment

Pregnant women with opioid use disorder in treatment throughout pregnancy and postpartum period

Women with opioid use disorder in a previous pregnancy who are receiving appropriate treatment and care preconceptionally

Infants with prenatal opioid exposure receiving appropriate neonatal assessment and care

Infants with prenatal opioid exposure linked to early intervention services

Infants with prenatal opioid exposure monitored for behavioral and learning disabilities

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